IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Hakan Lomryd, et al.

Title: PHARMACEUTICAL COMPOSITION AS SOLID DOSAGE FORM AND METHOD FOR MANUFACTURING THEREOF

Appl. No.: 10/626,857

Filing Date: July 25, 2003

Examiner: T. PAGE

Art Unit: 1615

PETITION TO MAKE NEW APPLICATION SPECIAL UNDER 37 C.F.R. 1.102 AND M.P.E.P. 708.02

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant hereby petitions to make special the captioned new patent application, which has not received any examination by the Examiner, in order to advance examination.

The following items are submitted in support of this petition:

(a) A Preliminary Amendment amending the claims to conform to those granted from the corresponding European patent application. Applicants believe that the claims presented are directed to a single invention. If the Patent Office determines otherwise, Applicants will make an election without traverse of the composition claims as a prerequisite to the grant of special status.

(b) A Statement that a pre-examination search was made by a foreign patent office, the European Patent Office, with regard to claims of the same or similar scope as the claims presented in the captioned application (as amended by the

Preliminary Amendment submitted concurrently herewith), for which special status is requested.

(c) One copy of each reference deemed most closely related to the subject matter encompassed by the claims, if the reference is not already of record. (Here the references are already of record).

(d) A Detailed Discussion of the references, pointing out with particularity how the claimed subject matter is patentable over the cited references.

(e) A Check in the amount of $130.00 for the required petition fee.

Please charge any additional fees required by this paper or credit any overpayment to Deposit Account No. 19-0741.

Respectfully submitted,

Date April 25, 2005 By _____

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STATEMENT & DETAILED DISCUSSION SUPPORTING PETITION TO MAKE NEW APPLICATION SPECIAL UNDER 37 C.F.R. 1.102 AND M.P.E.P. 708.02

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Set forth below are the Statement regarding pre-examination search and Detailed Discussion of the references required to support the accompanying Petition to make the captioned new patent application special.

STATEMENT REGARDING PRE-EXAMINATION SEARCH

The undersigned hereby states that a pre-examination search was made by a foreign patent office with regard to claims in a corresponding foreign application which are of the same or similar scope to the claims in the U.S. application for which special status is requested.

In particular, the European Patent Office conducted a search in corresponding EPC Patent Application No. 03 016 945.2 with regard to claims of the same or similar scope to the claims in the captioned application. (A copy of the European Search Report was submitted in the application with the Information Disclosure Statement filed August 18, 2004.) The EPC Patent Application was classified into International Classes A61K9/20; A61K38/11, and Technical Field A61K was searched. The Preliminary Amendment submitted herewith amends the instant claims to conform to those that will grant in EPC Patent Application No. 03 016 945.2. A copy of the claims that will be granted in Europe is attached as Appendix A, together with a copy of the Communication from the EPO stating that the claims will be granted.

DETAILED DISCUSSION OF REFERENCES

The European Search Report identified one reference deemed to be particularly relevant to the invention, U.S. 2002/0122817 ("Gabel"), and two references deemed to be particularly relevant if combined with other documents, U.S. Patent No. 5,047,398 (the '398 patent), and Williams, et al., J. Pharm. Sci. 78: 1025-34 (1989) ("Williams"). These references already have been submitted in the instant application via Information Disclosure Statements filed October 24, 2003 and August 18, 2004. The patentability of the claimed invention over these references is discussed with particularity below.

The present invention relates to solid dosage forms of desmopressin, or a pharmaceutically acceptable salt thereof. Desmopressin (also known as dDAVP) is useful, for example, in the treatment of primary nocturnal enuresis (bed-wetting) in children. Specification, pg. 1, ln. 7-14. The present invention provides solid dosage forms of desmopressin that offer substantial manufacturing advantages. Specification, pg. 3, ln. 8-25.

Specifically, Applicants found that using a lower amount of lubricant in the solid dosage form than is conventional achieves increased hardness and permits increased compressing speeds. Specification, pg. 3, ln. 8-15.

The claim set presented in the Preliminary Amendment submitted herewith includes two independent claims, claim 1 (directed to a pharmaceutical composition) and claim 19 (directed to a method of manufacture):

> 1. A pharmaceutical composition as a solid dosage form comprising desmopressin, or a pharmaceutically acceptable salt thereof, as a therapeutically active ingredient together with a pharmaceutically acceptable excipient, diluent or carrier, or mixture thereof, wherein the pharmaceutical composition is composed of a compressed granulate and contains lubricant in an amount of from 0.05 to 0.40 percent by weight of said pharmaceutical composition.
>
> 19. A method for the manufacturing of a pharmaceutical composition as a solid dosage form comprising desmopressin, or a pharmaceutically acceptable salt thereof, as a therapeutically active ingredient, wherein said method comprises the steps of:
>
> i) mixing desmopressin and an excipient, diluent or carrier, or mixture thereof, optionally in the presence of a wetting agent;
>
> ii) subjecting the resulting mixture to formation of a granulate, optionally in the presence of a wetting agent, suitable for compression into said solid dosage form;
>
> iii) optionally performing said mixing and/or formation of a granulate in the presence of at least one additive selected from a disintegrating agent, binder, flavoring agent, preservative, colorant and a mixture thereof;
>
> iv) optionally drying said granulate;
>
> v) compressing said granulate into said solid dosage form,

wherein lubricant is introduced so that the resulting pharmaceutical composition contains lubricant in an amount of from 0.05 to 0.40 percent by weight of said pharmaceutical composition.

This invention is not taught or suggested by any combination of Gabel, the '398 patent, or Williams.

1. Gabel

Gabel is directed to solid, instant release dosage forms that form a gel in aqueous media. Gabel discloses desmopressin in a long list of active agents that can be formulated in accordance with its teachings. Gabel does not teach or suggest a composition comprising desmopressin and from 0.05 to 0.40 percent by weight of a lubricant, as recited in the instant claims.

There is no general teaching in Gabel of using a specific amount of lubricant in its dosage forms. In the examples of Gabel that include magnesium stearate (a lubricant in accordance with the present invention), the magnesium stearate comprises 2.5 to 2.6 percent by weight of the composition. Moreover, those examples do not comprise desmopressin as the active agent. Thus, Gabel does not lead the skilled artisan to the present invention.

2. The '398 Patent

The '398 patent describes an oral dosage form of desmopressin. The patent teaches dosage forms comprising from 50 to 200 μg desmopressin and states that the composition "may be in any form suitable for oral administration including tablets, capsules and other forms known to those skilled in this art." '398 patent, col. 2, ln. 39-49. The patent indicates that other ingredients in addition to desmopressin can be included, such as "well known fillers and other inert constituents." '398 patent, col. 2, ln. 50-53.

There is no general teaching in the '398 patent of using a specific amount of lubricant in its dosage forms. In the Examples, the compositions comprise desmopressin, mannitol,

lactose, microcrystalline cellulose, crosslinked carboxymethylcellulose, talcum and magnesium stearate. '398 patent, col. 2, ln. 64-col. 3, ln. 7. Those compositions comprise 3.2 and 4.5 percent by weight lubricant. (Both the talcum and the magnesium stearate are lubricants in accordance with Applicant's invention. See, e.g., page 4, lines 27-35 of the instant specification.) Thus, the '398 patent does not lead the skilled artisan to the present invention.

3. Williams

Williams is directed to the compaction properties of microcrystalline cellulose and sodium sulphathiazole with talc or magnesium stearate. The reference indicates that those compounds are representative of a plastic excipient and a brittle drug, respectively. See, e.g., Abstract. The teachings of Williams are not relevant to the properties of desmopressin.

Desmopressin is an oligopeptide hormone that is an amorphous material. See, e.g., U.S. Patent No. 5,500,413, col. 1, ln. 34-36 (describing the amorphous characteristics of desmopressin) (copy attached in Appendix B). Thus, desmopressin does not have the properties of a brittle drug.

Even reading the teachings of Williams broadly would not suggest the present invention. For example, the data in Figure 1 of Williams show that tablet strength decreased with increasing magnesium stearate content, but was essentially constant over a range of talc content. Thus, Williams does not teach or suggest that controlling lubricant content per se can affect tablet strength. Moreover, Williams does not teach or suggest that the amount of lubricant recited in the instant claims would be advantageous.

No combination of the cited references would teach or suggest the present invention. Even taken together, Gabel, the '398 patent, and Williams do not teach or suggest a solid dosage form comprising desmopressin (or a pharmaceutically acceptable salt thereof) and from 0.05 to 0.40 percent by weight lubricant. Gabel and the '398 patent disclose (through

their examples) much higher lubricant contents, and Williams is directed to the characteristics of brittle drugs, not amorphous drugs like desmopressin.

In view of the foregoing, Applicants respectfully urge that the Petition to Make Special be granted, and that an early notice of Allowability be issued.

If there are any questions regarding this submission, the Patent Office is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

Date April 25, 2005 By Courtenay C. Brinckerhoff

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